REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and following remarks.

Claim 1 has been amended to limit the component (c).

Claims 1, 3, 4 and 6-9 are rejected under 35 USC 103 as unpatentable over Ogawa et al. in view of Fu et al., Cagle et al. and Miyagi et al. for the reasons set forth in the Official Action.

This ground of rejection is respectfully traversed as applied to the amended claims.

As described in the present specification, the purpose of the present invention is to provide a stable and clear aqueous solution preparation containing an aminoglycoside antibiotic or its pharmacologically acceptable salt and bromfenac or its pharmacologically acceptable salt (please see page 4, lines 9-12 of the specification).

By using limitation (c) in combination with limitations (a) and (b), a stable and clear aqueous solution preparation wherein no precipitation occurs can be obtained.

3.2 Cited prior art references

D1: Ogawa et al. (US 4,910,225)

D2: Fu et al. (US 5,414,011)

D3: Cagle et al. (US 6,440,964)

D4: Miyagi et al. (US 6,281,224)

(1) D1: Ogawa et al. (US 4,910,225)

D1 discloses a locally administrable therapeutic composition for inflammatory disease which is characterized by comprising benzoylphenylacetic acid, as an active ingredient.

However, it is neither disclosed nor suggested in D1 that an aminoglycoside antibiotic is used to prepare the therapeutic composition. The limitation (a) of the present invention is neither disclosed nor suggested in D1. Further, limitation (c) of the present invention is neither disclosed nor suggested in D1.

Of course, D1 neither discloses nor suggests that turbidity and suspension formation occurs in a combined aqueous solution preparation comprising bromfenac and an aminoglycoside antibiotic. Further, D1 neither discloses nor suggests that a stable and clear aqueous solution without causing precipitation can be provided by further adding

monoethanolamine or its pharmacologically acceptable salt, or nicotinamide to the aqueous solution preparation comprising bromfenac and an aminoglycoside antibiotic.

Thus, there is no mention nor suggestion about the purpose and effect of the present invention.

Therefore, the essential components, the purpose and effect of the present invention are neither disclosed nor suggested in D1.

Accordingly, the present invention is unobvious over D1.

(2) D2: Fu et al. (US 5,414,011)

D2 discloses an opthalmologically acceptable ketorolac formulation. The purpose of D2 is to provide a stable and clear formulation for ketrolac and quaternary ammonium compounds benzaikonium chloride (BAC). As described in D2, NSAIDs such as ketrolac have proven to be incompatible with quaternary ammonium compounds such as BAC because they can form a complex with NSAIDs, rendering the preservative less available to serve its function (for example, see column 1, lines 51-53 and column 2, lines 48-53 of D2).

In D2, to solve the above problem, octoxynol 40, a nonionic polyoxyethylated octylphenol surfactant, is added to the formulation containing ketrolac and BAC. Further it is disclosed in D2 that tobramycin is added to the formulation to reduce/prevent the bacterial infection.

However, in D2, there is no mention nor suggestion about limitations (b) and (c) recited in claim 1.

Further, the purpose of the present invention is quite different from that of D2.

Until the present invention, with respect to a combined aqueous solution preparation comprising bromfenac and an aminoglycoside antibiotic, stable combined preparations have not yet been known, due to the difficulty in formulation of the above aminoglycoside antibiotic with the non-steroidal antiinflammatory agent. For example, when tobramycin is combined with diclofenac sodium which is a non-steroidal antiinflammatory agent, there is a problem that precipitation or suspension formation occurs, making it difficult to prepare an aqueous solution preparation comprising an aminoglycoside antibiotic and a nonsteroidal anti-inflammatory agent (see page 2, line 29 to page 3, line 7 of the present specification).

However, it is neither disclosed no suggested in D2 that turbidity and suspension formation occurs by adding tobramycin to the solution comprising ketrolac.

Further, it is neither disclosed nor suggested in D2 that the turbidity and suspension occurred are dissolved by adding limitation (c) recited in claim 1 to the formulation and thereby, a stable and clear aqueous solution without causing precipitation can be provided.

Therefore, the essential components, the purpose and effect of the present invention are neither disclosed nor suggested in D2.

Accordingly, D2 neither discloses nor suggests the present invention and thereby, the present invention is unobvious over D2.

(3) D3: Cagle et al. (US 6,440,964)

D3 discloses ophthalmic, otic and nasal compositions containing a new class of antibiotics such as Moxifloxacin and an anti-inflammatory agent such as bromfenac. In D3, the antibiotics such as Moxifloxacin and the anti-inflammatory agent is combined only to treat a bacterial infection and a resultant inflammation.

However, it is neither disclosed nor suggested in D3 that (a) an aminoglycoside antibiotic and (c) monoethanolamine or its pharmacologically acceptable salt, or nicotinamide are added to the composition. Therefore, D3 neither discloses nor suggests limitations (a) and (c) of the present invention.

Further, D3 neither discloses nor suggests how to provide a clear and stable aqueous solution preparation. Thus, there is no mention nor suggestion in D3 about the purpose of the present invention and thereby, D3 cannot be combined with D1, D2 or D4.

The Examiner argues in the Office Action that D3 was cited to show that cyclooxygenase type I and type II inhibitors such as diclofenac, flurbiprofen, ketorolac, suprofen, bromfenac, and indomethacin can be used interchangeably.

However, D3 has disclosed so many other agents as NSAIA, and thereby, it would have been inconceivable to those skilled in the art to select bromfenac among such many NSAIAs disclosed in D3.

Accordingly, the present invention is unobvious over D3. Further, it is unreasonable to combine D3 with D1, D2 or D4 because the purpose of the present invention is quite different from that of D3.

(4) D4: Miyagi et al. (US 6,281,224)

D4 discloses an ophthalmic solution containing pranoprofen and organic amine such as tromethamine.

However, D4 neither discloses nor suggests bromfenac and an aminoglycoside antibiotic, limitations (a) and (b) of the present invention. Of course, D4 neither discloses nor suggests that turbidity and suspension formation occurs in a combined aqueous solution preparation comprising bromfenac and an aminoglycoside antibiotic.

Therefore, the essential components and the purpose of the present invention are neither disclosed nor suggested in D4.

It is understood from D4 that cloudiness in the preparation comprising pranoprofen, boric acid, sodium borate and benzalkonium chloride is dissolved by using tromethamine instead of boric acid and sodium borate (please see reference preparation 2 in Table 1 and reference preparation 1 in Table 2). However, D4 neither discloses nor suggests that a stable and clear aqueous solution without causing precipitation can be provided by further adding monoethanolamine or its pharmacologically acceptable salt, or nicotinamide to the aqueous solution preparation comprising bromfenac and an aminoglycoside antibiotic.

Therefore, the essential elements, the purpose and effect of the present invention are neither disclosed nor suggested in D4.

(5) Combination of D1 -D4

Applicant respectfully submits that the rejection is based upon an impermissible hindsight reconstruction of the claimed invention by selecting components of the claimed invention in the prior art to combine. The motivation to make such a claimed combination, however, is absent in the prior art and in the rejection.

As described above, the essential elements, the purpose and effect of the present invention are neither disclosed nor suggested in the combination of D1-D4. Therefore, it is not obvious to those skilled in the art to combine D1-D4.

Further, it is unreasonable to combine D3 with D1, D2 and D4 because the purpose of D3 is quite different from that of the present invention.

Accordingly, the present invention was inconceivable from Dl-D4 to those skilled in the art and is unobvious from these cited prior art references.

Favorable action on the merits is solicited.

Respectfully submitted,

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